

WHAT IS CLAIMED IS:

1. A vector comprising a viral vector, a viral vector nucleic acid, or a nucleic acid construct that comprises a viral vector nucleic acid sequence, said vector being capable of expressing an exogenous gene or exogenous nucleic acid sequences in a target cell of interest, said vector comprising a nucleic acid component or components which comprise:
 - i) one or more native promoter/enhancer regions in which at least one sequence segment has been modified,
 - ii) one or more non-native promoter/enhancers or a non-native promoter's gene or gene segment, and
 - iii) a native viral vector terminator or a processing signal or segment thereof, or both.
2. The viral vector of claim 1, wherein the vector further comprises a non-native terminator.
3. The viral vector of claim 1, comprising two or more modified sequence segments.
4. The viral vector of claim 1, wherein said modification comprises a substitution of a native sequence segment with a non-native sequence segment in said one or more promoter/enhancer regions of said vector.
5. The viral vector of claim 4, wherein the sequence segments in said substitution are approximately the same size.

6. The viral vector of claim 1, wherein said modification comprises a mutation selected from the group consisting of a point mutation, a deletion, an insertion, and a substitution, or a combination of any of the foregoing.

7. The viral vector of claim 1, wherein said viral vector is a retrovirus.

8. The viral vector of claim 1, wherein said terminator, or said processing signal, or both, include a polyadenylation signal.

9. The viral vector of claim 1, comprising a segment of said viral vector terminator or a segment of said processing signal, or both.

10. The viral vector of claim 1, wherein the function of said one or more promoter/enhancers have been reduced, inhibited or eliminated.

11. The viral vector of claim 1, wherein said one or more non-native promoters are capable of producing an RNA lacking a polyadenylation signal.

12. The viral vector of claim 11, wherein said one or more non-native promoters are selected from the group of genes consisting of snRNA, tRNA, and rRNA, or a combination of any of the foregoing.

13. The viral vector of claim 12, further comprising one or more gene or gene segment sequences of said snRNA, tRNA or rRNA gene or genes.

14. The viral vector of claims 12 or 13, wherein said snRNA is selected from the group consisting of U1, U2, U3, U4, U5, U6, U7, U8, U9, U10 and U11, or a combination of any of the foregoing.

15. The viral vector of claims 1, 12 or 13, wherein said one or more non-native promoter's gene or gene segment sequence have been modified.

16. The viral vector of claim 15, wherein said modification comprises a substitution or replacement of or addition to said one or more non-native promoter's gene sequence with said exogenous gene or an exogenous nucleic acid sequence.

17. A viral vector comprising a virus or viral portion having on a surface or an envelope thereof at least two components, one component for adsorption to a packaging cell line for said vector, and the other component for adsorption to a target cell for delivery of said vector.

18. The viral vector of claim 17, wherein both components are native to said viral vector.

19. The viral vector of claim 17, wherein said one component is native to the virus, and the other component is non-native to the virus.

20. The viral vector of claim 17, wherein both components are non-native to said viral vector.

21. The viral vector of claims 19 or 20, wherein said non-native component is selected or derived from the group consisting of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Herpes Simplex Virus (HSV), and Vesicular Stomatitis Virus (VSV), and a part or portion thereof, or a combination of any of the foregoing.

22. The viral vector of claim 21, wherein said HIV or part or portion thereof comprises gp120.

23. The viral vector of claim 21, wherein ~~said HBV or part or portion thereof, or said HCV or said part or portion thereof~~ comprises a surface antigen.

24. The viral vector of claim 17, wherein said viral vector comprises a retrovirus.

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26. The viral vector of claim 24, wherein said retrovirus comprises a murine retrovirus.

26. The viral vector of claims 18 or 19, wherein one of the components is ecotropic.

27. The viral vector of claims 18 or 19, wherein one of the components is amphotropic.

28. The viral vector of claim 17, wherein one or the other or both components are selected from the group consisting of a protein, an oligo- or polypeptide, a glycoprotein, a fused peptide, a recombinant peptide, a modified protein, or a combination of any of the foregoing.

29. A viral vector comprising a virus or viral portion thereof having on a surface or an envelope at least two components, the first component being native to the virus, and the second component characterized in that

- (i) it is non-native to said viral vector;
- (ii) it is capable of adsorption to a target cell of interest, and
- (iii) it is incapable of adsorption to a cell native for said viral vector.

30. The viral vector of claim 29, wherein said viral vector is a retrovirus.

31. The viral vector of claim 30, wherein said retrovirus is selected from the group consisting of a murine leukemia virus, a human immunodeficiency virus, a human T cell leukemia virus and a Gibbon ape leukemia virus, or a combination of any of the foregoing.

32. The viral vector of claim 29, wherein said non-native component is selected or derived from the group consisting of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Herpes Simplex Virus (HSV), and Vesicular Stomatitis Virus (VSV), and a part or portion thereof, or a combination of any of the foregoing.

33. The viral vector of claim 32, wherein said derived member comprises HIV gp120.

34. The viral vector of claim 32, wherein said derived member comprises HBV surface antigen or HCV surface antigen.

35. The viral vector of claim 29, wherein said target cell is selected from the group consisting of T cells, liver cells, bone marrow cells and epithelial cells, or a combination of any of the foregoing.

36. A vector selected from the group consisting of a (i) viral vector, (ii) a viral nucleic acid, and (iii) a nucleic acid construct, said vector comprising a non-native nucleic acid sequence coding for a segment, said segment being capable of integration into a target cell's genome, and said vector being capable of producing or introducing a first nucleic acid in said target cell,

said first nucleic acid being capable of producing a second nucleic acid that comprises a portion of said first nucleic acid, said second nucleic acid comprising said integration segment and being capable of expressing an exogenous gene or an exogenous nucleic acid sequence.

37. The vector of claim 36, wherein said vector comprises a viral vector and said integration segment is non-native to said viral vector.

38. The vector of claim 36, wherein said vector comprises a viral nucleic acid and said integration segment is non-native to said viral vector.

39. The vector of claim 36, wherein said viral vector (i) comprises adenovirus.

40. The viral vector of claim 36, wherein said first nucleic acid comprises a retrovirus and said second nucleic acid comprises adeno-associated virus (AAV).

41. The viral vector of claim 36, wherein said first nucleic acid comprises adeno-associated virus (AAV) and said second nucleic acid comprises a retrovirus.

42. The viral vector of claim 37, wherein said second nucleic acid sequence comprises retroviral LTR or adeno-associated virus.

43. A first vector selected from the group consisting of (i) a viral vector comprising a viral nucleic acid and a viral vector packaging component or components, (ii) a viral nucleic acid, and (iii) a nucleic acid construct,
wherein when introduced into a packaging cell said first vector is capable of producing a second vector selected from the group consisting of (a) a second viral vector, (b) a viral nucleic acid, and (c) a second nucleic acid construct, each being capable of expressing an exogenous gene or exogenous nucleic acid sequence in a target cell of interest,
wherein said first vector is capable of producing in said packaging cell said second vector, and
wherein said packaging cell is capable of providing one or more packaging components for said second viral nucleic acid,
wherein said second viral nucleic acid or said second nucleic acid construct is structurally different from said first (i) viral nucleic acid or said first (iii) nucleic acid construct, or more than one packaging component for said second viral vector is different from said first viral vector packaging component or components (ii), or both.

44. The first vector of claim 43, wherein said first vector comprises a retrovirus and said second vector comprises adeno-associated virus (AAV).

45. The first vector of claim 43, wherein said structural difference comprises a difference selected from the group consisting of the nucleic acid chemical nature, the nucleic acid form, the nucleic acid size, and functional elements, or a combination of any of the foregoing.

46. The first vector of claim 45, wherein said nucleic acid chemical nature, the second viral nucleic acid or the second nucleic acid is selected from the group consisting of RNA and DNA, and the (i) viral nucleic acid or the (iii) nucleic acid construct comprises a different member of said group.

47. The first vector of claim 45, wherein said nucleic acid form, the second viral nucleic acid or the second nucleic acid is selected from the group consisting of single-stranded, double-stranded and partially double-stranded, and the (i) viral nucleic acid or the (iii) nucleic acid construct comprises a different member of said group.

48. The first vector of claim 45, wherein said nucleic acid size, the second viral nucleic acid or the second nucleic acid comprises a segment of the (i) viral nucleic acid or the (iii) nucleic acid construct.

49. The first vector of claim 45, wherein said functional elements, the second viral nucleic acid or the second nucleic acid comprises one or more promoters, one or more enhancer regions, an integration segment and a terminator, or a portion or a segment or a combination of any of the foregoing, and the (i) viral nucleic acid or the (iii) nucleic acid construct comprises a different member of said group.

50. The first vector of claim 43, wherein said first vector comprises a retrovirus and said second vector comprises adeno-associated virus.

51. The first vector of claim 43, wherein said first vector comprises adeno-associated virus and said second vector comprises a retrovirus.

52. A packaging cell line for propagating the viral vector of claim 50, wherein said packaging cell line provides at least two packaging components for the surface or envelope of said viral vector.

53. The packaging cell line of claim 52, wherein said cell line is native to said viral vector.

54. The packaging cell line of claim 52, wherein said viral vector comprises a retrovirus.

55. The packaging cell line of claim 52, wherein said cell line is selected from the group consisting of NIH 3T3, U937, H9 and 293, or a combination of any of the foregoing.

56. The packaging cell line of claim 52, wherein any sequences for both the surface or envelope components are stably integrated in a chromosome or chromosomes of said packaging cell line.

57. The packaging cell line of claim 52, wherein a sequence of a surface or envelope component is stably integrated in a chromosome or chromosomes of said packaging cell line, and a sequence of another surface or envelope component is transiently expressed.

58. The packaging cell line of claim 52, wherein a sequence of said envelope component is stably integrated in a chromosome or chromosomes of said packaging cell line, and a sequence of said surface component is transiently expressed.

59. The packaging cell line of claim 52, wherein any sequences for both the surface or envelope components are transiently expressed.

60. Packaging cell line for propagating the viral vector of any of claims 19, 20 or 29, wherein said cell line is non-native to said viral vector component or components but native to said viral vector nucleic acid, wherein said packaging cell line expresses on its membrane or its surface a receptor or receptors or binding partner or partners for adsorption to said non-native component for said vector.

61. A process for producing the viral vector or viral vector nucleic acid of claim 1, said process comprising the steps of:

providing said vector of claim 1; and

introducing said vector into a packaging cell under conditions to produce said viral vector or said viral vector nucleic acid.

62. The process of claim 61, wherein said providing step or introducing step, the nucleic acid construct has been modified in a promoter/enhancer region.

63. The process of claim 61, wherein said providing step or introducing step, the nucleic acid construct has been modified in a non-native promoter.

64. The process of claim 61, wherein said nucleic acid construct is capable of stable integration into the genome of said packaging cell line.

65. The process of claim 61, wherein said nucleic acid construct has been modified by means of an episome.

66. The process of claim 61, wherein said nucleic acid construct has been modified by means of transient expression.

67. A packaging cell line for propagating a viral vector independent of a helper virus, said viral vector comprising a nucleic acid component and a non-nucleic acid component, wherein said sequence or sequences for the viral vector nucleic acid component is stably integrated in the genome of said cell line, and said sequence or sequences for the non-nucleic acid component of said viral vector are introduced into said packaging cell line by a means selected from the group consisting of transient expression, episomal expression, stably integrated expression, or a combination of any of the foregoing.

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Add B2
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